

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket No: 124-688

In re patent application of

Elmore, Michael J. et al.

Serial No. 08/981,087

Filed: May 27, 1998

For: TYPE F BOTULINUM TOXIN AND USE THEREOF



STATEMENT TO SUPPORT FILING AND SUBMISSION IN
ACCORDANCE WITH 37 C.F.R. §§ 1.821-1.825

Assistant Commissioner for Patents
Washington, D.C. 20231
Box SEQUENCE

Sir:

In connection with a Sequence Listing submitted concurrently herewith, the undersigned hereby states that:

1. the submission, filed herewith in accordance with 37 C.F.R. § 1.821(g), does not include new matter;

2. the content of the attached paper copy and the attached computer readable copy of the Sequence Listing, submitted in accordance with 37 C.F.R. § 1.821(c) and (e), respectively, are the same; and

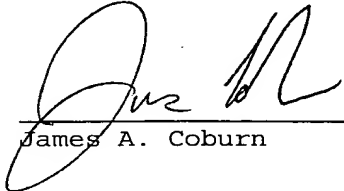
3. all statements made herein of their own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United

Serial No. 08/981,087

States Code and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

Respectfully submitted,

Sept. 4, 1999
Date


James A. Coburn

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SEQUENCE LISTING



(1) GENERAL INFORMATION:

(i) APPLICANT: Elmore, Michael J.
Mauchline, Margaret L.
Minton, Nigel P.
Pasechnik, Vladimir A.
Titball, Richard W.

(ii) TITLE OF INVENTION: TYPE F BOTULINUM TOXIN AND USE THEREOF

(iii) NUMBER OF SEQUENCES: 6

(iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: NIXON & VANDERHYE P.C.
(B) STREET: 1100 North Glebe Rd. 8th floor
(C) CITY: Arlington
(D) STATE: VA
(E) COUNTRY: USA
(F) ZIP: 22201-4741

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER: US 08/981,087
(B) FILING DATE: 27-MAY-1998
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: PCT/GB96/01409
(B) FILING DATE: 12-JUN-1996

(viii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: GB 9511909.5
(B) FILING DATE: 12-JUN-1995

(ix) ATTORNEY/AGENT INFORMATION:

(A) NAME: Crawford, Arthur R.
(B) REGISTRATION NUMBER: 25,327
(C) REFERENCE/DOCKET NUMBER: 124-688

(x) TELECOMMUNICATION INFORMATION:

(A) TELEPHONE: 703-816-4000
(B) TELEFAX: 703-816-4100

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 431 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:

Ref #2

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Ser	Tyr	Thr	Asn	Asp	Lys	Ile	Leu	Ile	Leu	Tyr	Phe	Asn	Lys	Leu	Tyr	1	5	10	15
Lys	Lys	Ile	Lys	Asp	Asn	Ser	Ile	Leu	Asp	Met	Arg	Tyr	Glu	Asn	Asn	20	25	30	
Lys	Phe	Ile	Asp	Ile	Ser	Gly	Tyr	Gly	Ser	Asn	Ile	Ser	Ile	Asn	Gly	35	40	45	
Asp	Val	Tyr	Ile	Tyr	Ser	Thr	Asn	Arg	Asn	Gln	Phe	Gly	Ile	Tyr	Ser	50	55	60	
Ser	Lys	Pro	Ser	Glu	Val	Asn	Ile	Ala	Gln	Asn	Asn	Asp	Ile	Ile	Tyr	65	70	75	80
Asn	Gly	Arg	Tyr	Gln	Asn	Phe	Ser	Ile	Ser	Phe	Trp	Val	Arg	Ile	Pro	85	90	95	
Lys	Tyr	Phe	Asn	Lys	Val	Asn	Leu	Asn	Asn	Glu	Tyr	Thr	Ile	Ile	Asp	100	105	110	
Cys	Ile	Arg	Asn	Asn	Asn	Ser	Gly	Trp	Lys	Ile	Ser	Leu	Asn	Tyr	Asn	115	120	125	
Lys	Ile	Ile	Trp	Thr	Leu	Gln	Asp	Thr	Ala	Gly	Asn	Asn	Gln	Lys	Leu	130	135	140	
Val	Phe	Asn	Tyr	Thr	Gln	Met	Ile	Ser	Ile	Ser	Asp	Tyr	Ile	Asn	Lys	145	150	155	160
Trp	Ile	Phe	Val	Thr	Ile	Thr	Asn	Asn	Arg	Leu	Gly	Asn	Ser	Arg	Ile	165	170	175	
Tyr	Ile	Asn	Gly	Asn	Leu	Ile	Asp	Glu	Lys	Ser	Ile	Ser	Asn	Leu	Gly	180	185	190	
Asp	Ile	His	Val	Ser	Asp	Asn	Ile	Leu	Phe	Lys	Ile	Val	Gly	Cys	Asn	195	200	205	
Asp	Thr	Arg	Tyr	Val	Gly	Ile	Arg	Tyr	Phe	Lys	Val	Phe	Asp	Thr	Glu	210	215	220	
Leu	Gly	Lys	Thr	Glu	Ile	Glu	Thr	Leu	Tyr	Ser	Asp	Glu	Pro	Asp	Pro	225	230	235	240
Ser	Ile	Leu	Lys	Asp	Phe	Trp	Gly	Asn	Tyr	Leu	Leu	Tyr	Asn	Lys	Arg	245	250	255	

Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln Asn
 260 265 270
 Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys Pro
 275 280 285
 Asn Ile Phe Ser Asn Thr Arg Leu Tyr Thr Gly Val Glu Val Ile Ile
 290 295 300
 Arg Lys Asn Gly Ser Thr Asp Ile Ser Asn Thr Asp Asn Phe Val Arg
 305 310 315 320
 Lys Asn Asp Leu Ala Tyr Ile Asn Val Val Asp Arg Asp Val Glu Tyr
 325 330 335
 Arg Leu Tyr Ala Asp Ile Ser Ile Ala Lys Pro Glu Lys Ile Ile Lys
 340 345 350
 Leu Ile Arg Thr Ser Asn Ser Asn Asn Ser Leu Gly Gln Ile Ile Val
 355 360 365
 Met Asp Ser Ile Gly Asn Asn Cys Thr Met Asn Phe Gln Asn Asn Asn
 370 375 380
 Gly Gly Asn Ile Gly Leu Leu Gly Phe His Ser Asn Asn Leu Val Ala
 385 390 395 400
 Ser Ser Trp Tyr Tyr Asn Asn Ile Arg Lys Asn Thr Ser Ser Asn Gly
 405 410 415
 Cys Phe Trp Ser Phe Ile Ser Lys Glu His Gly Trp Gln Glu Asn
 420 425 430

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 144 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Ser Tyr Thr Asn Asp Lys Ile Leu Ile Leu Tyr Phe Asn Lys Leu Tyr
 1 5 10 15
 Lys Lys Ile Lys Asp Asn Ser Ile Leu Asp Met Arg Tyr Glu Asn Asn
 20 25 30
 Lys Phe Ile Asp Ile Ser Gly Tyr Gly Ser Asn Ile Ser Ile Asn Gly
 35 40 45

Asp Val Tyr Ile Tyr Ser Thr Asn Arg Asn Gln Phe Gly Ile Tyr Ser
 50 55 60
 Ser Lys Pro Ser Glu Val Asn Ile Ala Gln Asn Asn Asp Ile Ile Tyr
 65 70 75 80
 Asn Gly Arg Tyr Gln Asn Phe Ser Ile Ser Phe Trp Val Arg Ile Pro
 85 90 95
 Lys Tyr Phe Asn Lys Val Asn Leu Asn Asn Glu Tyr Thr Ile Ile Asp
 100 105 110
 Cys Ile Arg Asn Asn Asn Ser Gly Trp Lys Ile Ser Leu Asn Tyr Asn
 115 120 125
 Lys Ile Ile Trp Thr Leu Gln Asp Thr Ala Gly Asn Asn Gln Lys Leu
 130 135 140

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 144 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Val Phe Asn Tyr Thr Gln Met Ile Ser Ile Ser Asp Tyr Ile Asn Lys
 1 5 10 15
 Trp Ile Phe Val Thr Ile Thr Asn Asn Arg Leu Gly Asn Ser Arg Ile
 20 25 30
 Tyr Ile Asn Gly Asn Leu Ile Asp Glu Lys Ser Ile Ser Asn Leu Gly
 35 40 45
 Asp Ile His Val Ser Asp Asn Ile Leu Phe Lys Ile Val Gly Cys Asn
 50 55 60
 Asp Thr Arg Tyr Val Gly Ile Arg Tyr Phe Lys Val Phe Asp Thr Glu
 65 70 75 80
 Leu Gly Lys Thr Glu Ile Glu Thr Leu Tyr Ser Asp Glu Pro Asp Pro
 85 90 95
 Ser Ile Leu Lys Asp Phe Trp Gly Asn Tyr Leu Leu Tyr Asn Lys Arg
 100 105 110
 Tyr Tyr Leu Leu Asn Leu Leu Arg Thr Asp Lys Ser Ile Thr Gln Asn
 115 120 125

Ser Asn Phe Leu Asn Ile Asn Gln Gln Arg Gly Val Tyr Gln Lys Pro
 130 135 140

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 143 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Asn	Ile	Phe	Ser	Asn	Thr	Arg	Leu	Tyr	Thr	Gly	Val	Glu	Val	Ile	Ile	1	5	10	15
Arg	Lys	Asn	Gly	Ser	Thr	Asp	Ile	Ser	Asn	Thr	Asp	Asn	Phe	Val	Arg	20	25	30	
Lys	Asn	Asp	Leu	Ala	Tyr	Ile	Asn	Val	Val	Asp	Arg	Asp	Val	Glu	Tyr	35	40	45	
Arg	Leu	Tyr	Ala	Asp	Ile	Ser	Ile	Ala	Lys	Pro	Glu	Lys	Ile	Ile	Lys	50	55	60	
Leu	Ile	Arg	Thr	Ser	Asn	Ser	Asn	Asn	Ser	Leu	Gly	Gln	Ile	Ile	Val	65	70	75	80
Met	Asp	Ser	Ile	Gly	Asn	Asn	Cys	Thr	Met	Asn	Phe	Gln	Asn	Asn	Asn	85	90	95	
Gly	Gly	Asn	Ile	Gly	Leu	Leu	Gly	Phe	His	Ser	Asn	Asn	Leu	Val	Ala	100	105	110	
Ser	Ser	Trp	Tyr	Tyr	Asn	Asn	Ile	Arg	Lys	Asn	Thr	Ser	Ser	Asn	Gly	115	120	125	
Cys	Phe	Trp	Ser	Phe	Ile	Ser	Lys	Glu	His	Gly	Trp	Gln	Glu	Asn	130	135	140		

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1293 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

TCATATACTA ATGATAAAAT TCTAATTTTA TATTTTAATA AATTATATAA AAAAATTAAA	60
GATAACTCTA TTTTAGATAT GCGATATGAA AATAATAAAT TTATAGATAT CTCTGGATAT	120
GGTTCAAATA TAAGCATTAA TGGAGATGTA TATATTTATT CAACAAATAG AAATCAATTT	180
GGAATATATA GTAGTAAGCC TAGTGAAGTT AATATAGCTC AAAATAATGA TATTATATAC	240
AATGCTAGAT ATCAAAATTT TAGTATTAGT TTCTGGGTAA GGATTCCTAA ATACTTCAAT	300
AAAGTGAATC TTAATAATGA ATATACTATA ATAGATTGTA TAAGGAATAA TAATTCAGGA	360
TGGAAAATAT CACTTAATTA TAATAAAATA ATTTGGACTT TACAAGATAC TGCTGGAAAT	420
AATCAAAAAC TAGTTTTTAA TTATACACAA ATGATTAGTA TATCTGATTA TATAAATAAA	480
TGGATTTTTG TAACTATTAC TAATAATAGA TTAGGCAATT CTAGAATTTA CATCAATGGA	540
AATTTAATAG ATGAAAAATC AATTTCGAAT TTAGGTGATA TTCATGTTAG TGATAATATA	600
TTATTTAAAA TTGTTGGTTG TAATGATACA AGATATGTTG GTATAAGATA TTTTAAAGTT	660
TTTGATACGG AATTAGGTAA AACAGAAATT GAGACTTTAT ATAGTGATGA GCCAGATCCA	720
AGTATCTTAA AAGACTTTTG GGGAAATTAT TTGTTATATA ATAAAAGATA TTATTTATTG	780
AATTTACTAA GAACAGATAA GTCTATTACT CAGAATTCAA ACTTTCTAAA TATTAATCAA	840
CAAAGAGGTG TTTATCAGAA ACCAAATATT TTTTCCAACA CTAGATTATA TACAGGAGTA	900
GAAGTTATTA TAAGAAAAAA TGGATCTACA GATATATCTA ATACAGATAA TTTTGTTAGA	960
AAAAATGATC TGGCATATAT TAATGTAGTA GATCGTGATG TAGAATATCG GCTATATGCT	1020
GATATATCAA TTGCAAAACC AGAGAAAATA ATAAAATTAA TAAGAACATC TAATTCAAAC	1080
AATAGCTTAG GTCAAATTAT AGTTATGGAT TCAATAGGAA ATAATTGCAC AATGAATTTT	1140
CAAAACAATA ATGGGGGCAA TATAGGATTA CTAGGTTTTC ATTCAAATAA TTTGGTTGCT	1200
AGTAGTTGGT ATTATAACAA TATACGAAAA AATACTAGCA GTAATGGATG CTTTGGAGT	1260
TTTATTTCTA AAGAGCATGG ATGGCAAGAA AAC	1293

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1313 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

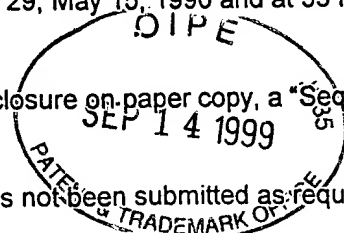
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

GGATCCATAT GTCTTACACT AACGACAAAA TCCTGATCCT GTACTTCAAC AAAGTGTACA 60
 AAAAAATCAA AGACAACTCT ATCCTGGACA TCGGTTACGA AAACAACAAA TTCATCGACA 120
 TCTCTGGCTA TGGTTCTAAC ATCTCTATCA ACGGTGACGT CTACATCTAC TCTACTAACC 180
 GCAACCAGTT CGGTATCTAC TCTTCTAAAC CGTCTGAAGT AAACATCGCT CAGAACAACG 240
 ACATCATCTA CAACGGTCGT TACCAGAACT TCTCTATCTC TTTCTGGGTT CGTATCCCGA 300
 AATACTTCAA CAAAGTTAAC CTGAACAACG AATACACTAT CATCGACTGC ATCCGTAACA 360
 ACAACTCTGG TTGGAAAATC TCTCTGAACT ACAACAAAAT CATCTGGACT CTGCAGGACA 420
 CTGCTGGTAA CAACCAGAAA CTGGTTTTCA ACTACACTCA GATGATCTCT ATCTCTGACT 480
 ACATTAATAA ATGGATCTTC GTTACTATCA CTAACAACCG TCTGGGTAAC TCTCGTATCT 540
 ACATCAACGG TAACCTGATC GATGAAAAAT CTATCTCTAA CCTGGGTGAC ATCCACGTTT 600
 CTGACAACAT CCTGTTCAAA ATCGTTGGTT GCAACGACAC GCGTTACGTT GGTATCCGTT 660
 ACTTCAAAGT TTTCGACACT GAACTGGGTA AAAGTGAAT CGAAACTCTG TACTCTGACG 720
 AACCGGACCC GTCTATCCTG AAAGACTTCT GGGGTAACTA CCTGCTGTAC AACAAACGTT 780
 ACTACCTGCT GAACCTGCTC CGGACTGACA AATCTATCAC TCAGAACTCT AACTTCTCTGA 840
 ACATCAACCA GCAGCGTGGT GTTTATCAGA AACCTAATAT CTTCTCTAAC ACTCGTCTGT 900
 ACACTGGTGT TGAAGTTATC ATCCGTAAAA ACGGTTCTAC TGACATCTCT AACACTGACA 960
 ACTTCGTACG TAAAAACGAC CTGGCTTACA TCAACGTTGT TGACCGTGAC GTTGAATACC 1020
 GTCTGTACGC TGACATCTCT ATCGCTAAAC CGGAAAAAAT CATCAAAGT ATCCGTACTT 1080
 CTAAGTCTAA CAACTCTCTG GGTCAGATCA TCGTTATGGA CTCGATCGGT AACAACTGCA 1140
 CTATGAAGTT CCAGAACAAC AACGGTGGTA ACATCGGTCT GCTGGGTTTC CACTCTAACA 1200
 ACCTGGTTGC TTCTTCTTGG TACTACAACA ACATCCGTAA AAACACTTCT TCTAACGGTT 1260
 GCTTCTGGTC TTTCATCTCT AAAGAACACG GTTGGCAGGA AAAGTAATCT AGA 1313

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- ☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other: _____



Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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